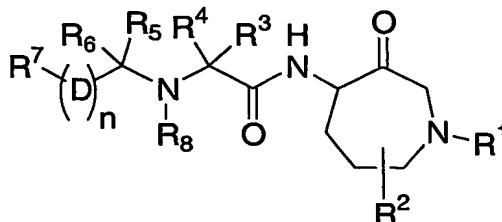


WHAT IS CLAIMED IS:

1. A compound of the formula:



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wherein R¹ is hydrogen, C₁₋₆ alkyl, -SO₂R⁹, -C(O)R⁹ or arylC₁₋₆alkyl;

R² is hydrogen, C₁₋₆ alkyl or C₃₋₆ cycloalkyl;

- 10 R³ is hydrogen, C₁₋₆ alkyl or C₂₋₆ alkenyl wherein said alkyl and alkenyl groups are optionally substituted with C₃₋₆ cycloalkyl or halo;

R⁴ is hydrogen, C₁₋₆ alkyl or C₂₋₆ alkenyl wherein said alkyl and alkenyl groups are optionally substituted with C₃₋₆ cycloalkyl or halo;

- 15 or R³ and R⁴ can be taken together with the carbon atom to which they are attached to form a C₃₋₈ cycloalkyl ring, C₅₋₈ cycloalkenyl ring, or five to seven membered heterocyclyl wherein said cycloalkyl, cycloalkenyl and heterocyclyl groups are optionally substituted with C₁₋₆ alkyl, halo, hydroxyalkyl, hydroxy, alkoxy or keto;

R⁵ is selected from hydrogen or C₁₋₆ alkyl substituted with 1-6 halo;

- 20 R⁶ is aryl, heteroaryl, C₁₋₆ haloalkyl, arylalkyl or heteroarylalkyl, wherein said aryl, heteroaryl, arylalkyl and heteroarylalkyl groups are optionally substituted with halo, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₆ cycloalkyl, -SR⁹, -SR¹², -SOR⁹, -SOR¹², -SO₂R⁹, -SO₂R¹², -SO₂CH(R¹²)(R¹¹), -OR¹², -N(R¹⁰)(R¹¹) or cyano;

- 25 D is C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkenyl, aryl, heteroaryl, C₃₋₈ cycloalkyl or heterocyclyl wherein said aryl, heteroaryl, cycloalkyl and heterocyclyl groups, which may be monocyclic or bicyclic, are optionally substituted on either the carbon or the heteroatom with one to five substituents selected from C₁₋₆ alkyl, halo or keto;

R⁷ is hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyloxy, halo, nitro, cyano, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocyclyl, -C(O)OR¹⁰, -C(O)OSi[CH(CH₃)₂]₃, -OR¹⁰, -C(O)R¹⁰, -R¹⁰C(O)R⁹, -C(O)R⁹, -C(O)N(R¹²)(R¹²), -C(O)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)OH, -SR¹², -SR⁹, -R¹⁰SR⁹, -R⁹, -C(R⁹)₃, -C(R¹⁰)(R¹¹)N(R⁹)₂, -NR¹⁰C(O)NR¹⁰S(O)₂R⁹, -SO₂R¹², -SO(R¹²), -SO₂R⁹, -SO₂N(R^c)(R^d), -SO₂CH(R¹⁰)(R¹¹), -SO₂N(R¹⁰)C(O)(R¹²), -SO₂(R¹⁰)C(O)N(R¹²)₂, -OSO₂R¹⁰, -N(R¹⁰)(R¹¹), -N(R¹⁰)C(O)N(R¹⁰)(R⁹), -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)OR¹⁰, -N(R¹⁰)SO₂(R¹⁰), -C(R¹⁰)(R¹¹)NR¹⁰C(R¹⁰)(R¹¹)R⁹, -C(R¹⁰)(R¹¹)N(R¹⁰)R⁹, -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)SC(R¹⁰)(R¹¹)R⁹, R¹⁰S-, -C(R^a)(R^b)NR^aC(R^a)(R^b)₂, -C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)C(R^a)(R^b)N(R^a)(R^b), -C(O)C(R^a)(R^b)N(R^a)(R^b), -C(R^a)(R^b)N(R^a)C(O)R⁹, -C(O)C(R^a)(R^b)S(R^a)(R^b) or C(R^a)(R^b)C(O)N(R^a)(R^b); wherein said groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁₋₆ alkyl, halo, keto, cyano, haloalkyl, hydroxyalkyl, -OR⁹, -O(aryl), -NO₂, -NH₂, -NHS(O)₂R⁸, -R⁹SO₂R¹², SO₂R¹², SO(R¹²), SO₂N(R^c)(R^d), SO₂N(R¹⁰)C(O)(R¹²), -C(R¹⁰)(R¹¹)N(R¹⁰)(R¹¹), -C(R¹⁰)(R¹¹)OH, -COOH, -C(R^a)(R^b)C(O)N(R^a)(R^b), -N(R¹⁰)C(R¹⁰)(R¹¹), -NH(CH₂)₂OH, -NHC(O)OR¹⁰, Si(CH₃)₃, heterocyclyl, aryl or heteroaryl;

R⁸ is hydrogen or C₁₋₆ alkyl;
or R⁴ and R⁸ or can be taken together with any of the atoms to which they may be attached or are between them to form a 4-10 membered heterocyclyl ring system wherein said ring system, which may be monocyclic or bicyclic, is optionally substituted with C₁₋₆ alkyl, halo, hydroxyalkyl, hydroxy, keto, OR¹⁰, SR¹⁰ or N(R¹⁰)₂;

R⁹ is selected from the group consisting of hydrogen, aryl, aryl(C₁₋₄) alkyl, heteroaryl, heteroaryl(C₁₋₄)alkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkyl(C₁₋₄)alkyl, and heterocyclyl(C₁₋₄)alkyl wherein said groups can be optionally substituted with halo or alkoxy;

R¹⁰ is hydrogen or C₁₋₆ alkyl

R¹¹ is hydrogen or C₁₋₆ alkyl;

R¹² is hydrogen or C₁₋₆ alkyl which is optionally substituted with halo, alkoxy, cyano, -NR¹⁰ or -SR¹⁰;

R^a is hydrogen, C₁₋₆ alkyl, (C₁₋₆ alkyl)aryl, (C₁₋₆ alkyl)hydroxyl, -O(C₁₋₆ alkyl), hydroxyl, halo, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocyclyl, wherein said alkyl, aryl, heteroaryl, C₃₋₈

cycloalkyl and heterocyclyl can be optionally substituted on either the carbon or the heteroatom with C₁₋₆ alkyl or halo;

R^b is hydrogen, C₁₋₆ alkyl, (C₁₋₆ alkyl)aryl, (C₁₋₆ alkyl)hydroxyl, alkoxy, hydroxyl, halo, aryl, heteroaryl, C₃₋₈ cycloalkyl, heterocyclyl, wherein said alkyl, aryl, heteroaryl, C₃₋₈ cycloalkyl and heterocyclyl can be optionally substituted on either the carbon or the heteroatom with C₁₋₆ alkyl or halo;

or R^a and R^b can be taken together with the carbon atom to which they are attached or are between them to form a C₃₋₈ cycloalkyl ring or C₃₋₈ heterocyclyl ring wherein said 3-8 membered ring system may be optionally substituted with C₁₋₆ alkyl and halo;

R^c is hydrogen or C₁₋₆ alkyl which is optionally substituted with halo or OR⁹;

R^d is hydrogen or C₁₋₆ alkyl which is optionally substituted with halo or OR⁹;

or R^c and R^d can be taken together with the nitrogen atom to which they are attached or are between them to form a C₃₋₈ heterocyclyl ring which is optionally substituted with C₁₋₆ alkyl, halo hydroxyalkyl, hydroxy, alkoxy or keto;

n is independently selected from an integer from zero to three;

and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

2. The compound of Claim 2 wherein R³ and R⁴ are each independently selected from hydrogen or C₁₋₄ alkyl; or R³ and R⁴ can be taken together with the carbon atom to which they are attached to form a six membered cycloalkyl ring system, and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

3. The compound of Claim 1 wherein R⁵ is C₁₋₆alkyl substituted with 1-6 halo and R⁶ is C₁₋₆ alkyl substituted with 1-6 halo; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

4. The compound of Claim 1 wherein R⁵ is hydrogen and R⁶ is C₁₋₆ alkyl substituted with 1-6 halo; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

5. The compound of Claim 1 wherein R⁵ is hydrogen and R⁶ is aryl or heteroaryl wherein said aryl or heteroaryl are optionally substituted with halo or -SO₂R¹²; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

5 6. The compound of Claim 1 wherein R⁴ and R⁸ or can be taken together with any of the atoms to which they may be attached or are between them to form a 4-10 membered heterocyclyl ring system wherein said ring system, which may be monocyclic or bicyclic, is optionally substituted with C₁₋₆ alkyl, halo, hydroxyalkyl, hydroxy, keto, -OR¹⁰, -SR¹⁰ or -N(R¹⁰)₂; and the pharmaceutically acceptable salts, stereoisomers and N-oxide
10 derivatives thereof.

7. The compound of Claim 6 wherein R⁴ and R⁸ can be taken together with any of the atoms to which they may be attached or are between them to form a 5 or 6 membered heterocyclyl ring system wherein said ring system, is optionally substituted with C₁₋₆ alkyl, halo,
15 hydroxyalkyl, hydroxy, keto, -OR¹⁰, -SR¹⁰ or -N(R¹⁰)₂; and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

8. The compound of Claim 1 selected from:
*N*¹-[3-Oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]-*N*²-{(1*S*)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)-
20 1,1'-biphenyl-4-yl]ethyl}-L-leucinamide, and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof.

9. A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier.

25 10. A pharmaceutical composition made by combining a compound according to any one of Claims 1 to 8 and a pharmaceutically acceptable carrier.

30 11. A process for making a pharmaceutical composition comprising combining a compound according to Claim 1 and a pharmaceutically acceptable carrier.

12. A method of inhibiting cathepsin activity in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

13. The method according to Claim 13 wherein the cathepsin activity is Cathepsin K activity.

14. A method of treating or preventing a disease selected from: osteoporosis, glucocorticoid induced osteoporosis, Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, rheumatoid arthritis, osteoarthritis, periprosthetic osteolysis, osteogenesis imperfecta, metastatic bone disease, hypercalcemia of malignancy or multiple myeloma in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

15. A method of treating or preventing bone loss in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

16. A method of treating or preventing osteoporosis in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

17. A method of treating cathepsin dependent conditions in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

18. A pharmaceutical composition comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

19. A method of treating osteoporosis comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

20. A method of treating bone loss comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

21. A pharmaceutical composition comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an osteoblast anabolic agent, and the pharmaceutically acceptable salts and mixtures thereof.

22. A compound of any one of Claims 1 to 8, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, for use in inhibiting cathepsin activity, such as cathepsin K activity.

23. Use of a compound of any one of Claims 1 to 8, or a pharmaceutically acceptable salt, stereoisomer or N-oxide derivative thereof, in the manufacture of a medicament for treating or preventing a disease set forth in Claim 14.